This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

/ IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

FENT COOPERATION TREA

NOTIFICATION OF ELECTION (PCT Rule 61.2) Date of mailing (day/month/year) 14 January 2000 (14.01.00) International application No. PCT/GB99/01557 PBA3/DD8815PWO International filling date (day/month/year) 17 May 1999 (17.05.99) Applicant OLIVER, Stephen, George et al 1. The designated Office is hereby notified of its election made: \[\begin{array}{c c c c c c c c c c c c c c c c c c c		From the INTERNATIONAL BUREAU
United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMÉRIQUE International application No. PCT/GB99/01557 International filing date (day/month/year) 17 May 1999 (17.05.99) Applicant OLIVER, Stephen, George et al 1. The designated Office is hereby notified of its election made: X in the demand filed with the International Preliminary Examining Authority on: 13 December 1999 (13.12.99) in a notice effecting later election filed with the International Bureau on: 2. The election X was was not made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).	PCT	То:
International application No. PCT/GB99/01557 International filing date (day/month/year) 17 May 1999 (17.05.99) Applicant OLIVER, Stephen, George et al 1. The designated Office is hereby notified of its election made: X in the demand filed with the International Preliminary Examining Authority on: 13 December 1999 (13.12.99) in a notice effecting later election filed with the International Bureau on: 2. The election X was was not made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).		United States Patent and Trademark Office Box PCT Washington, D.C.20231
International filing date (day/month/year) 17 May 1999 (17.05.99) Applicant OLIVER, Stephen, George et al 1. The designated Office is hereby notified of its election made: X in the demand filed with the International Preliminary Examining Authority on: 13 December 1999 (13.12.99) in a notice effecting later election filed with the International Bureau on: 2. The election X was was not made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).		in its capacity as elected Office
Applicant OLIVER, Stephen, George et al 1. The designated Office is hereby notified of its election made: X in the demand filed with the International Preliminary Examining Authority on: 13 December 1999 (13.12.99) in a notice effecting later election filed with the International Bureau on: 2. The election X was was not made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).		PBA3/DO88155PWO
1. The designated Office is hereby notified of its election made: X in the demand filed with the International Preliminary Examining Authority on: 13 December 1999 (13.12.99)		
1. The designated Office is hereby notified of its election made: X in the demand filed with the International Preliminary Examining Authority on: 13 December 1999 (13.12.99) in a notice effecting later election filed with the International Bureau on: 2. The election X was was not was not was not was not was not was 2.2(b).		
	in a notice effecting later election filed with the Int 2. The election X was was not made before the expiration of 19 months from the priori	er 1999 (13.12.99) ernational Bureau on:
The International Bureau of WIPO 34, chemin des Colombettes Authorized officer H. Zhou	The International Bureau of WIPO	Authorized officer

Telephone No.: (41-22) 338.83.38

Facsimile No.: (41-22) 740.14.35

1211 Geneva 20, Switzerland

TENT COOPERATION TRE. Y

	From th	e INTERNATIONAL BU	JREAU	
PCT				
NOTIFICATION OF THE RECORDING OF A CHANGE (PCT Rule 92bis.1 and		ATKINSON, Peter, Birch Marks & Clerk Sussex House		
Administrative Instructions, Section 422)	83-85 Mosley Street Manchester M2 3LG ROYAUME-UNI			
Date of mailing (day/month/year) 09 October 2000 (09.10.00)				
Applicant's or agent's file reference PBA3/DO88155PWO		IMPORTANT NOTII	FICATION	
International application No. PCT/GB99/01557	1	ay 1999 (17.05.99)	ear)	
The following indications appeared on record concerning: The applicant the inventor	the agent	the commo	n representative	
Name and Address UNIVERSITY OF MANCHESTER		State of Nationality GB	State of Residence GB	
Institute of Science and Technology P.O. Box 88 Manchester M60 1QD United Kingdom	-	Telephone No.		
		Teleprinter No.	* * * * * * * * * * * * * * * * * * *	
2. The International Bureau hereby notifies the applicant that t X the person the name the add	_	the nationality	the residence	
Name and Address THE VICTORIA UNIVERSITY OF MANCHESTER		State of Nationality GB	State of Residence GB	
Oxford Road Manchester M13 9PL		Telephone No.		
United Kingdom		Facsimile No.		
		Teleprinter No.		
3. Further observations, if necessary:				
4. A copy of this notification has been sent to:		•		
X the receiving Office		the designated Offices of	concerned	
the International Searching Authority the International Preliminary Examining Authority	[]	the elected Offices cond	cerned	
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized o	officer Sean Taylor		
Facsimile No.: (41-22) 740.14.35	Telephone N	No.: (41-22) 338.83.38		



PCT

REC'D	0 4	SEP	2000	
WIPC)		PCT	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

16

(PCT Article 36 and Rule 70)

PBA/DO	_		FOR FURTHER ACT	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/4			
					· · ·	La	
Internationa			International filing date (day	y/month	/year)	Priority date (day/month/year)	
PCT/GB99/01557 17/05/1999 16/05/1998							
Internationa C12N15/		ent Classification (IPC) or na	tional classification and IPC				
Applicant							
UNIVER	SITY	OF MANCHESTER IN	ISTITUTE OF et al.				
		ational preliminary exami smitted to the applicant a		repared	by this Inte	rnational Preliminary Examining Authority	
2. This f	REPO	ORT consists of a total of	8 sheets, including this c	over sl	heet.		
(:	see R		07 of the Administrative In			ectifications made before this Authority ne PCT).	
3. This r	eport	contains indications rela	iting to the following items	s :			
1	⊠	Basis of the report					
11	\boxtimes	Priority					
III \Box Non-establishment of opinion with regard to					entive step	and industrial applicability	
IV ⊠ Lack of unity of invention							
V A Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement							
VI 🗆 Certain documents cited							
VII		Certain defects in the ir	nternational application				
VIII	Ø	Certain observations or	n the international applica	ition			
Date of sub	missio	on of the demand		Date of	completion of	this report	
						00	

Date of submission of the demand	Date of completion of this report	
13/12/1999	3 0. 08. 00	
Name and mailing address of the international preliminary examining authority:	Authorized officer	CLEAN COLO M. LA. LA.
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d	Marinoni, J-C	(1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.
Fax: +49 89 2399 - 4465	Telephone No. +49 89 2399 8563	St. S TOWN. ISING.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01557

1. This report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.): Description, pages: 1-38 as originally filed Claims, No.: 1-21 as originally filed 22-38 with telefax of 11/08/2000 Drawings, sheets: as originally filed 1/9-9/9 2. The amendments have resulted in the cancellation of: ☐ the description, pages: ☐ the claims, Nos.: ☐ the drawings, sheets: 3. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)): 4. Additional observations, if necessary: **II.** Priority 1.

This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested: copy of the earlier application whose priority has been claimed.

☐ translation of the earlier application whose priority has been claimed.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01557

2.		This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.
Th	us fo	or the purposes of this report, the international filing date indicated above is considered to be the relevant date
3.	Add	ditional observations, if necessary:
	see	separate sheet
IV	. Lac	k of unity of invention
1.	In r	esponse to the invitation to restrict or pay additional fees the applicant has:
		restricted the claims.
		paid additional fees.
		paid additional fees under protest.
		neither restricted nor paid additional fees.
2.	⊠	This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3.	Thi	s Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
		complied with.
	Ø	not complied with for the following reasons:
		see separate sheet
4.		nsequently, the following parts of the international application were the subject of international preliminary amination in establishing this report:
	×	all parts.
		the parts relating to claims Nos

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/01557

V. Reasoned stat m nt under Articl 35(2) with regard to nov lty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes:

Claims 1-38

No: Claims NONE

Inventive step (IS)

Yes: C

Claims 1-35, 37, 38

No:

Claims 36

Industrial applicability (IA)

Yes:

Claims 1-38

No:

Claims NONE

2. Citations and explanations

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item II

Priority

The document ZHANG et al. 'Down-regulation of the expression of PKC1 and SRB1/PSA1/VIG9, two genes involved in cell wall integrity in *Saccharomyces cerevisiae*, causes flocculation.' MICROBIOLOGY, Vol. 145, No. Pt 2, February 1999, pages 309-316, has been cited as a P document.

The International Preliminary Examination Authority considers the priority of the present application to be valid. Therefore, this document is not taken into consideration for the establishement of the following opinion. However, some of the documents therein cited are considered to be relevant and are fully citable.

Re Item IV

Lack of unity of invention

Reference is made to the following document:

D1: J. CELL BIOL., Vol. 116, No. 5, 1992, pages 1221-1229, Levin and Bartlett-Heubusch 'Mutants in the S. cerevisiae PKC1 gene display a cell specific osmotic stability defect'

Reference is made to the following document which was not cited in the search report (cited in Zhang et al. 1999).

- **D2**: Zhang, N., PhD thesis, University of Manchester-Institute of Science and Technology, 1997.
- 1. The separate inventions/groups of invention are:
 - (i) Yeast cells wherein the SRB1 and PKC1 genes are each under the control of a heterologous (inducible) promoter, method of regulating yeast cell lysis and method of fermentation using said yeast cells (claims 1-14, 32-34, 37, 38),
 - (ii) Yeast cells wherein the PKC1 gene is under the control of a heterologous inducible promoter, method of regulating yeast cell flocculation using said yeast cells (claims 15-23, 35)
 - (iii) Yeast cells wherein the SRB1 gene is under the control of a heterologous promoter, method of fermentation using said yeast cells (claims 24-31, 36)

- **EXAMINATION REPORT SEPARATE SHEET**
- 2. They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:
 - (a) the technical feature linking group (i) and (ii) of inventions resides in yeast cells comprising the PKC1 gene under the control of an inducible heterologous promoter; this technical feature is not novel (see **D1**).
 - (b) the technical feature linking group (i) and (iii) of inventions resides in yeast cells comprising the SRB1 gene under the control of a heterologous promoter (i.e. subject-matter of claim 36); this subject-matter is not novel (see the grounds for this objection)
 - (c) the technical feature linking group (ii) and (iii) of inventions resides in yeast cells; this feature is obviously not new.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- Claim 1 is directed to a yeast cell containing the SRB1/PSA1 gene and the PKC1 gene or functional derivatives thereof each operatively linked to a heterologous inducible promoter.
 - None of the available document discloses nor suggests such cells or methods using said cells. Therefore, the subject-matter of claim 1 meets the requirements of Article 33(2) PCT concerning novelty and Article 33(3) PCT concerning inventive step.
 - Consequently, claims 2-14 and 32-34 also meet these requirements of the PCT.
- 2. Claim 15 is directed to a method of regulating yeast cell flocculation comprising growing yeast cells containing the PKC1 gene operatively linked to an inducible promoter. None of the available document discloses nor suggests a link between PKC1 and yeast flocculation.
 - None of the available documents neither discloses nor suggests such a method. Therefore, the subject-matter of **claim 15** meets the requirement of Article 33(2) PCT concerning novelty and of Article 33(3) PCT concerning inventive step.

EXAMINATION REPORT - SEPARATE SHEET

Consequently, dependent claims 16-23 also meet these requirements of the PCT.

3. Claim 24 is directed to a method of fermentation comprising growing yeast cells containing the SRB1/PSA1 gene under the control of a heterologous promoter. None of the available documents neither discloses nor suggests such a method. Therefore, claim 24 meets the requirement of Article 33(3) PCT concerning inventive step.

Consequently, dependent claims 25-31 also meet these requirements of the PCT.

4. Claim 35 is directed to yeast cells comprising the PKC1 gene under the control of an inducible heterologous promoter and selected from two cell lines transformed with specific constructs, and a third cell line. None of the available documents suggests that the specific cells lines containing one of the specific constructs could or should be obtained.

Therefore, the subject-matter of **claim 35** meets the requirements of Article 33(3) PCT concerning inventive step.

5. Claim 36 is directed to yeast cells comprising the SRB1 gene under the control of a heterologous promoter.

Zhang et al. (1999) refers (see page 310, lines 45-55) to document **D2** which appears to disclose yeast cells transformed with vectors containing the SRB1/PSA1 gene under the control of the MET3 promoter.

Therefore, the subject-matter of **claim 36** does not meet the requirements of Article 33(2) PCT concerning novelty.

Re Item VIII

Certain observations on the international application

- 1. Many claims refer to names of plasmids or cells lines which appear to be arbitrary denomination which have no defined meaning for the skilled person. Said claims (see claims 6-8, 20-22, 29-31, 35) are therefore not clear (Article 6 PCT).
- 2. Many claims refer to "functional derivatives" of the SRB1 and/or PKC1 genes.

 None of these functional derivatives is examplified in the application as filed. The

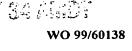


INTERNATIONAL PRELIMINARY

International application No. PCT/GB99/01557

EXAMINATION REPORT - SEPARATE SHEET

scope of protection afforded by the term "functional derivative" is not fully clear (Article 6 PCT). Furthermore, none of the examples in the application as filed refers specifically to one of such "functional derivatives" (Article 6 PCT). It appears that the caracterisation of such "functional derivatives" useful in the claimed processes would place undue burden on the skilled person (Article 5 PCT).



- 22. The method according to any one of claims 15 to 20 wherein the yeast cells are ZO123 or ZO124 transformed with the *PKC1* gene or functional derivative thereof operatively linked to an inducable promoter.
- 23. The method according to any one of claims 15 to 22 for increasing the sedimentation of yeast cells or cell ghosts / debris form a medium within which the yeast cells are grown.
- 23. A method of fermentation comprising growing yeast cells containing the *SRB1/PSA1* gene or functional derivative thereof operatively linked to a heterologous promoter in a growth medium in which *SRB1/PSA1* expression is regulated by the heterologous promoter whereby said cells flocculate.
- 24. The method according to claim 23 wherein the yeast cell is a strain of Saccharomyces cerevisiae
- 25. The method according to claim 23 wherein the yeast cell is a strain of *Pichia pastoris*, *Hansenula polymorpha* or *Kluyveromyces lactis*.
- 26. The method according to any one of claims 23 25 wherein the *SRB1/PSA1* gene or functional derivative thereof is operatively linked to a methionine regulated promoter.
- 27. The method according to claim 26 wherein the methionine regulated promoter is pMET3.
- 28. The method according to claim 27 wherein the *SRB1/PSA1* gene or functional derivatives thereof operatively linked to an inducable promoter is derived from the recombinant vector SRB1.9e.

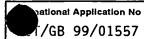
- 29. The method according to claim 28 wherein the yeast cells are ZO-125.
- 30. The method according to claim 28 wherein the yeast cells are FY23SRB1MET3.
- A method of fermentation comprising growing yeast cells containing the *SRB1/PSA1* and *PKC1* gene or functional derivatives thereof operatively linked to a heterologous promoter in a growth medium in which *SRB1/PSA1* and *PKC1* expression is regulated by the heterologous promoter whereby said cells flocculate.
- 32. The method according to claim 31 wherein the cells are cells according to any one of claims 1 8.
- 33. The method according to claim 31 wherein the cells contain the *PKC1* gene or a functional derivative thereof operatively linked to a heterologous inducable promoter and the *SRB1/PSA1* gene or a functional derivative thereof operatively linked to a heterologous promoter.
- 34. A yeast cell containing the *PKC1* gene or functional derivatives thereof operatively linked to a heterologous inducable promoter.
- 35. A yeast cell containing the *SRB1/PSA1* gene or functional derivatives thereof operatively linked to a heterologous promoter.
- 36. A yeast cell containing the *PKC1* gene or a functional derivative thereof operatively linked to a heterologous inducable promoter and the *SRB1/PSA1* gene or a functional derivative thereof operatively linked to a heterologous promoter.
- 37. A yeast cell according to any one of claims 34 36 wherein the promoter or promoters is/are pMET3.

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER see Notification of	of Transmittal of International Search Report				
PBA3/D088155PW0	ACTION (Form PCT/ISA/2	220) as well as, where applicable, item 5 below.				
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)				
PCT/GB 99/01557	17/05/1999	16/05/1998				
Applicant						
UNITED STITE OF MANGUESTED	1					
UNIVERSITY OF MANCHESTER	et al.	·				
This International Search Report has been according to Article 18. A copy is being tra	n prepared by this International Searching Autransmitted to the International Bureau.	nority and is transmitted to the applicant				
This International Search Report consists It is also accompanied by	of a total of sheets. a copy of each prior art document cited in this	report.				
Basis of the report						
	international search was carried out on the bas less otherwise indicated under this item.	sis of the international application in the				
the international search w Authority (Rule 23.1(b)).	vas carried out on the basis of a translation of the	he international application furnished to this				
*		nternational application, the international search				
	onal application in written form.					
	ernational application in computer readable form	n.				
	furnished subsequently to this Authority in written form.					
	this Authority in computer readble form.					
	osequently furnished written sequence listing do is filed has been furnished.	oes not go beyond the disclosure in the				
X the statement that the info	rmation recorded in computer readable form is	s identical to the written sequence listing has been				
2. Certain claims were four	nd unsearchable (See Box I).					
3. Unity of invention is laci	king (see Box II).					
4. With regard to the title,						
the text is approved as su	* ''					
	hed by this Authority to read as follows:	VEACT				
KEGULATED EXPRESSION C	OF PKC AND/OR SRB1/PSA1 IN Y	/EAST				
5. With regard to the abstract,	•					
the text is approved as sul						
the text has been establish within one month from the	hed, according to Rule 38.2(b), by this Authorit a date of mailing of this international search rep	y as it appears in Box III. The applicant may, ort, submit comments to this Authority.				
6. The figure of the drawlngs to be publi	shed with the abstract is Figure No.	-				
as suggested by the applic	cant.	None of the figures.				
because the applicant faile	ed to suggest a figure.					
because this figure better	characterizes the invention.					

INTERNATIONAL SEARCH REPORT



a. classi IPC 6	FICATION OF SUBJECT C12N15/81	C12N15/54	C12N1/19	/.	/(C12N1/19,0	C12R1:865)
According to	o International Patent Cla	ssification (IPC) or to boti	h national classificat	ion and IPC	i	
<u>-</u> _	SEARCHED					
Minimum do	cumentation searched (C12N C12R	classification system follo	wed by classification	symbols)		
Documentat	ion searched other than	minimum documentation	to the extent that suc	ch documer	nts are included in the	e fields searched
Electronic d	ata base consulted during	g the international search	(name of data base	and, whe	e practical, search tei	rms used)
C. DOCUME	ENTS CONSIDERED TO	BE RELEVANT				
Category °	Citation of document, w	vith indication, where app	ropriate, of the relev	ant passag	es	Relevant to claim No.
P,X	expression genes invo Saccharomy flocculati MICROBIOLO vol. 145,	GY, no. Pt 2, 999 (1999-02) 1 <i>'</i>	SRBI/PSA1/\ wall integr e, causes , pages 309	/IG9, f	CWO	1-37
<u> </u>	·	in the continuation of box	: C .	X Pat	ent family members a	re listed in annex.
"A" docume consid "E" earlier of filing d "L" docume which citation "O" docume other r "P" docume later th	ered to be of particular re locument but published o ate nt which may throw doub is cited to establish the pr n or other special reason ent referring to an oral dis neans	ate of the art which is no elevance in or after the international ts on priority claim(s) or ublication date of another (as specified) closure, use, exhibition of international filing date be ed	et al ") ") or ut	or prior cited to inventic documer cannot involve documer cannot documer ments, in the a documer Date of	ty date and not in con understand the princi in of particular relevan be considered novel con an inventive step whe at of particular relevan be considered to invole ont is combined with o such combination beis	
Name and n	NL - 2280 HV Rijsw	ice, P.B. 5818 Patentlaar rijk 040, Tx. 31 651 epo nl,	12		ed officer	

1

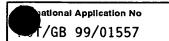
INTERNATIONAL SEARCH REPORT



Category* Citation of Occurrents, with including where appropriate, of the relevant passages Y BELDA F. & ZARATE V.: "Isolation and characterization of Schizosaccharomyces pombe fragile mutants" YEAST, vol. 12, 1996, pages 555-564, XP000852922 / the whole document A 1-22, 24-37 Y W0 94 03609 A (IMP CANCER RES TECH :PARKER PETER JOSEPH JACQUES (GB): GOODE NIGEL) 17 February 1994 (1994-02-17) abstract page 16 -page 18 claims 1-4 A W0 92 01798 A (UNIV MANCHESTER) 1-37 A W0 92 01798 A (UNIV MANCHESTER) 1-37 A RECH S.B. ET AL.: "Complementation of the Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GENET, vol. 21, 1992, pages 339-344, XP002122385 the whole document A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 the whole document A CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document -/	0./0	MIA-) POCHMENTS CONSIDERED TO BE ESTABLE	<u></u>	/ 0155/			
Y BELDA F. & ZARATE V.: "Isolation and characterization of Schizosaccharomyces pombe fragile mutants" YEAST, vol. 12, 1996, pages 555-564, XP000852922 / the whole document A 1-22, 24-37 W WO 94 03609 A (IMP CANCER RES TECH; PARKER PETER JOSEPH JACQUES (GB); GOODE NIGEL) 17 February 1994 (1994-02-17) abstract page 16 -page 18 claims 1-4 A 1-22, 24-37 A WO 92 01798 A (UNIV MANCHESTER) 1-37 A FECH S.B. ET AL.: "Complementation of the Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GEMET., vol. 21, 1992, pages 339-344, XP002122385 the whole document A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 / the whole document A CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document							
characterization of Schizosaccharomyces pomble fragile mutants" YEAST, vol. 12, 1996, pages 555-564, XP000852922 / the whole document 1-22, 24-37 W0 94 03609 A (IMP CANCER RES TECH ;PARKER PETER JOSEPH JACQUES (GB); GOODE NIGEL) 17 February 1994 (1994-02-17) abstract page 16 -page 18 claims 1-4 A	Calegory	onation of accument, with indication, where appropriate, of the relevant passages		nelevant to dalm No.			
A Vol. 12, 1996, pages 555-564, XP000852922 / the whole document 1-22, 24-37 WO 94 03609 A (IMP CANCER RES TECH ; PARKER PETER JOSEPH JACQUES (GB); GOODE NIGEL) 17 February 1994 (1994-02-17) abstract page 16 -page 18 claims 1-4 A WO 92 01798 A (UNIV MANCHESTER) 1-37 6 February 1992 (1992-02-06) abstract A RECH S.B. ET AL.: "Complementation of the Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GENET., vol. 21, 1992, pages 339-344, XP002122385 the whole document A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 / the whole document A CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document	Y	characterization of Schizosaccharomyces pombe fragile mutants"		23			
Y WO 94 03609 A (IMP CANCER RES TECH ; PARKER PETER JOSEPH JACQUES (GB); GOODE NIGEL) 17 February 1994 (1994-02-17) abstract page 16 -page 18 claims 1-4 A WO 92 01798 A (UNIV MANCHESTER) 6 February 1992 (1992-02-06) abstract A RECH S.B. ET AL.: "Complementation of the Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GENET., vol. 21, 1992, pages 339-344, XP002122385 the whole document A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 the whole document A CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document	_	vol. 12, 1996, pages 555-564, XP000852922 🗸					
PETER JOSEPH JACQUES (GB); GOODE NIGEL) 17 February 1994 (1994-02-17) abstract page 16 -page 18 claims 1-4 A	A	·					
A WO 92 01798 A (UNIV MANCHESTER) 6 February 1992 (1992-02-06) abstract A RECH S.B. ET AL.: "Complementation of the Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GENET., vol. 21, 1992, pages 339-344, XP002122385* the whole document A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 / the whole document A CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document	Y	PETER JOSEPH JACQUES (GB); GOODE NIGEL) 17 February 1994 (1994-02-17)		23			
A Wo 92 01798 A (UNIV MANCHESTER) 6 February 1992 (1992-02-06) abstract A RECH S.B. ET AL.: "Complementation of the Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GENET., vol. 21, 1992, pages 339-344, XP002122385* the whole document A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 / the whole document A CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document				,			
A RECH S.B. ET AL.: "Complementation of the Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GENET., vol. 21, 1992, pages 339-344, XP002122385 the whole document A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 the whole document CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 the whole document	A						
Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GENET., vol. 21, 1992, pages 339-344, XP002122385* the whole document A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 / the whole document A CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document	A	6 February 1992 (1992-02-06)		1-37			
A STATEVA L.I. ET AL.: "Cloning and characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991–08), pages 4235–4243, XP002122386 / the whole document A CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998–04–15), pages 345–349, XP000852924 / the whole document	A	Saccharomyces cerevisiae srb1-1 mutation: an autoselection system for stable plasmid maintenance" CURR. GENET., vol. 21, 1992, pages 339-344, XP002122385	·	1-37			
characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 / the whole document CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document		 · · · .		1.07			
CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell cycle" FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document	A	characterization of a gene which determines osmotic stability in Saccharomyces cerevisiae" MOL. CELL. BIOL., vol. 11, no. 8, August 1991 (1991-08), pages 4235-4243, XP002122386 /		1-3/			
FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 / the whole document	A	CARO L.H.P. ET AL.: "Transcription of multiple cell wall protein-encoding genes in Saccahromyces cerevisiae is differentially regulated during the cell		1-37			
		FEMS MICROBIOL. LETTERS, vol. 161, no. 2, 15 April 1998 (1998-04-15), pages 345-349, XP000852924 /					
		-/					
l l							

1

INTERNATIONAL SEARCH REPORT



A STATEVA L.I. ET AL.: "Polyploid fragile strains of Saccharomyces cerevisiae — a novel source of proteins for nutritional purposes" (VEAST, vol. 4, no. 3, September 1988 (1988-09), pages 219-225, XPD00852925 / the whole document A VERNA J.: "A family of genes required for maintenance of cell wall integrity and for the stress response in Saccharomyces cerevisiae" PROC. NATL. ACAD. SCI. USA, vol. 94, December 1997 (1997-12), pages 13804-13809, XPD02122387 / the whole document A KLIS F M: "REVIEW: CELL WALL ASSEMBLY IN YEAST" YEAST, 68, CHICHESTER, SUSSEX, vol. 10, page 851-869 XPD00196331 / ISSN: 0749-503X A WO 96 02629 A (UNIV MADRID COMPLUTENSE / ;NOMBELA CANO CESAR (ES); ALVAREZ ALVAREZ) 1 February 1996 (1996-02-01) abstract A SHANKAR C.S. ET AL.: "MIG1 overexpression causes flocculation in Saccharomyces cerevisiae" MICROBIOLOGY, vol. 142, no. Pt 9, 1996, pages 2663-2667, XPD02122388 / the whole document A US 5 716 808 A (RAYMOND CHRISTOPHER K) 10 February 1998 (1998-02-10) abstract A WO 88 10308 A (WHITTHEAD BIOMEDICAL INST) 1-37 29 December 1988 (1988-12-29) abstract				0155/
A STATEVA L.I. ET AL.: "Polyploid fragile strains of Saccharomyces cerevisiae — a novel source of proteins for nutritional purposes" YEAST, vol. 4, no. 3, September 1988 (1988-09), pages 219-225, XP000852925 / the whole document A VERNA J.: "A family of genes required for maintenance of cell wall integrity and for the stress response in Saccharomyces cerevisiae" PROC. NATL. ACAD. SCI. USA, vol. 94, December 1997 (1997-12), pages 13804-13809, XP002122387 / the whole document A KLIS F M: "REVIEW: CELL WALL ASSEMBLY IN YEAST, GB, CHICHESTER, SUSSEX, vol. 10, page 851-869 XP000196331 / ISSN: 0749-503X A WO 96 02629 A (UNIV MADRID COMPLUTENSE / ;NOMBELA CANO CESAR (ES); ALVAREZ ALVAREZ) 1 February 1996 (1996-02-01) abstract A SHANKAR C.S. ET AL.: "MIGI overexpression causes flocculation in Saccharomyces cerevisiae" MICROBIOLOGY, vol. 142, no. Pt 9, 1996, pages 2663-2667, XP002122388 / the whole document A US 5 716 808 A (RAYMOND CHRISTOPHER K) 1-37 in February 1998 (1998-02-10) abstract A WO 88 10308 A (WHITEHEAD BIOMEDICAL INST) 29 December 1988 (1988-12-29) abstract	C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT		
strains of Saccharomyces cerevisiae — a novel source of proteins for nutritional purposes" YEAST, vol. 4, no. 3, September 1988 (1988-09), pages 219-225, XP000852925 ~ the whole document A VERNA J.: "A family of genes required for maintenance of cell wall integrity and for the stress response in Saccharomyces cerevisiae" PROC. NATL. ACAD. SCI. USA, vol. 94, December 1997 (1997-12), pages 13804-13809, XP002122387 ~ the whole document A KLIS F M: "REVIEW: CELL WALL ASSEMBLY IN YEAST" YEAST, GB, CHICHESTER, SUSSEX, vol. 10, page 851-869 XP000196331 / ISSN: 0749-503X A WO 96 02629 A (UNIV MADRID COMPLUTENSE / ;NOMBELA CANO CESAR (ES); ALVAREZ ALVAREZ) 1 February 1996 (1996-02-01) abstract A SHANKAR C.S. ET AL.: "MIG1 overexpression causes flocculation in Saccharomyces cerevisiae" MICROBIOLOGY, vol. 142, no. Pt 9, 1996, pages 2663-2667, XP002122388 / the whole document A US 5 716 808 A (RAYMOND CHRISTOPHER K) 10 February 1998 (1998-02-10) abstract A WO 88 10308 A (WHITEHEAD BIOMEDICAL INST) / 29 December 1988 (1988-12-29) abstract	Category °	Citation of document, with indication, where appropriate, of the relevant passages	F	Relevant to claim No.
maintenance of cell wall integrity and for the stress response in Saccharomyces cerevisiae" PROC. NATL. ACAD. SCI. USA, vol. 94, December 1997 (1997–12), pages 13804–13809, XPO02122387 r the whole document A KLIS F M: "REVIEW: CELL WALL ASSEMBLY IN YEAST" YEAST, GB, CHICHESTER, SUSSEX, vol. 10, page 851–869 XPO00196331 r ISSN: 0749–503X A WO 96 02629 A (UNIV MADRID COMPLUTENSE r ; NOMBELA CANO CESAR (ES); ALVAREZ ALVAREZ) 1 February 1996 (1996–02–01) abstract A SHANKAR C.S. ET AL.: "MIG1 overexpression causes flocculation in Saccharomyces cerevisiae" MICROBIOLOGY, vol. 142, no. Pt 9, 1996, pages 2663–2667, XPO02122388 r the whole document A US 5 716 808 A (RAYMOND CHRISTOPHER K) 10 February 1998 (1998–02–10) abstract A WO 88 10308 A (WHITEHEAD BIOMEDICAL INST) 29 December 1988 (1988–12–29) abstract	A	strains of Saccharomyces cerevisiae a novel source of proteins for nutritional purposes" YEAST, vol. 4, no. 3, September 1988 (1988-09), pages 219-225, XP000852925		1-37
YEAST, GB, CHICHESTER, SUSSEX, vol. 10, page 851-869 XP000196331 / ISSN: 0749-503X A WO 96 02629 A (UNIV MADRID COMPLUTENSE / ;NOMBELA CANO CESAR (ES); ALVAREZ ALVAREZ) 1 February 1996 (1996-02-01) abstract A SHANKAR C.S. ET AL.: "MIG1 overexpression causes flocculation in Saccharomyces cerevislae" MICROBIOLOGY, vol. 142, no. Pt 9, 1996, pages 2663-2667, XP002122388 / the whole document A US 5 716 808 A (RAYMOND CHRISTOPHER K) 1-37 10 February 1998 (1998-02-10) abstract A WO 88 10308 A (WHITEHEAD BIOMEDICAL INST) 1-37 29 December 1988 (1988-12-29) abstract	A	maintenance of cell wall integrity and for the stress response in Saccharomyces cerevisiae" PROC. NATL. ACAD. SCI. USA, vol. 94, December 1997 (1997-12), pages 13804-13809, XP002122387 #		1-37
; NOMBELA CANO CESAR (ES); ALVAREZ ALVAREZ) 1 February 1996 (1996-02-01) abstract A SHANKAR C.S. ET AL.: "MIG1 overexpression causes flocculation in Saccharomyces cerevisiae" MICROBIOLOGY, vol. 142, no. Pt 9, 1996, pages 2663-2667, XP002122388/ the whole document A US 5 716 808 A (RAYMOND CHRISTOPHER K) 10 February 1998 (1998-02-10) abstract A WO 88 10308 A (WHITEHEAD BIOMEDICAL INST) 29 December 1988 (1988-12-29) abstract	A	YEAST" YEAST,GB,CHICHESTER, SUSSEX, vol. 10, page 851-869 XP000196331		1-37
causes flocculation in Saccharomyces cerevisiae" MICROBIOLOGY, vol. 142, no. Pt 9, 1996, pages 2663-2667, XP002122388/ the whole document A US 5 716 808 A (RAYMOND CHRISTOPHER K) 10 February 1998 (1998-02-10) abstract WO 88 10308 A (WHITEHEAD BIOMEDICAL INST) 29 December 1988 (1988-12-29) abstract	A	;NOMBELA CANO CESAR (ES); ALVAREZ ALVAREZ) 1 February 1996 (1996-02-01)		1-37
10 February 1998 (1998-02-10) abstract WO 88 10308 A (WHITEHEAD BIOMEDICAL INST) 29 December 1988 (1988-12-29) abstract	A	causes flocculation in Saccharomyces cerevisiae" MICROBIOLOGY, vol. 142, no. Pt 9, 1996, pages 2663-2667, XP002122388/		1-37
29 December 1988 (1988-12-29) abstract	Α .	10 February 1998 (1998-02-10)		1-37
	A	29 December 1988 (1988-12-29) abstract 		1-37

1

INTERNATIONAL SEARCH REPORT

ational Application No /GB 99/01557

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to daim No.
1	DATABASE GENBANK 'Online! Accession No. X06413, 12 September 1993 (1993-09-12) CHEREST H. ET AL.: "Yeast MET3 gene for ATP sulphurylase" XP002122389/ cited in the application the whole document & CHEREST H. ET AL.: "The Saccharomyces cerevisiae MET3 gene: nucleotide sequence and relationship of the 5' non-coding region to that of MET25." MOL. GEN. GENET., vol. 210, no. 2, 1987, pages 307-313,	1-37
		·
-		
	•	
	•	

1

INTERNATIONAL SEARCH REPORT

tion on patent family members

	pational Application No
ĺ	GB 99/01557

Patent document cited in search report		Publication date		atent family nember(s)	Publication date
WO 9403609	Α	17-02-1994	EP JP	0658202 A 8503124 T	21-06-1995 09-04-1996
WO 9201798	Α	06-02-1992	AU	8296291 A	18-02-1992
WO 9602629	A	01-02-1996	ES AU	2092439 A 3078795 A	16-11-1996 16-02-1996
US 5716808	A	10-02-1998	AU CA CA EP EP WO US EP US	1158297 A 7673796 A 2237039 A 2237120 A 0889966 A 0862640 A 9717450 A 9717451 A 5965389 A 0920525 A 5854039 A	29-05-1997 29-05-1997 15-05-1997 15-05-1997 13-01-1999 09-09-1998 15-05-1997 15-05-1997 12-10-1999 09-06-1999 29-12-1998
WO 8810308	Α	29-12-1988	US	5063154 A	05-11-1991

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY	PCT				
To: MARKS & CLERK Attn. ATKINSON,Peter Birch. Sussex House 83-85 Mosley Street MANCHESTER M2 3LG UNITED KINGDOM	COMMUNICATION IN CASES FOR WHICH NO OTHER FORM IS APPLICABLE				
	Date of mailing (day/month/year) 20/12/1999				
Applicant's or agent's file reference PBA3/D088155PW0	REPLY DUE See paragraph 1 below				
International application No. PCT/GB 99/ 01557	International filing date (day/month/year) 17/05/1999				
Applicant UNIVERSITY OF MANCHESTER et al.					
1. REPLY DUE within					

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Authorized officer

Andria Overbeeke-Siepkes